Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/pvj41360

EVALUATING THE ACCURACY OF INTRAOPERATIVE FROZEN SECTIONS FOR MARGIN ASSESSMENT IN ORAL CANCER SURGERY: A STUDY FROM A TERTIARY CARE HOSPITAL

Pankaj Chauhan[1*], Surabhi Pandey[2], Akanksha[3], Tanu Agrawal[4].

[1*]Junior Resident, Department of Pathology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh.
[2]Professor, Department of Pathology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh.
[3]Senior resident, Department of Pathology, Shaheed Hasan Khan Mewati Government Medical College & Hospital, Nuh, Haryana.
[4]Professor and Head, Department of Pathology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh.

***Corresponding author:** Dr Pankaj Chauhan
*Junior resident, Department of Pathology Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh. Email: pankajchauhan55@gmail.com

ABSTRACT

Background: Complete excision of malignant cells offers the best chance of cure in oral cancer, but microscopic tumor spread cannot be detected visually or by palpation. Hence, intraoperative frozen section analysis is commonly used to assess surgical margins, providing rapid diagnosis, margin evaluation, and guidance on malignancy status and lymph node dissection.

OBJECTIVE: We aimed to evaluate the role of frozen section diagnosis as a guide in resection of surgical margins of oral cancer.

MATERIAL AND METHOD: This retrospective study included 52 patients (264 margins) with oral carcinoma who underwent surgical resection at SRMS-IMS. Frozen sections were examined immediately for margins and later compared with hematoxylin and eosin-stained paraffin sections. Patients with prior oral cancer, previous treatments, or no positive histopathology were excluded. Margins were classified as positive (tumor present), close (between 1 - 5 mm) or negative (≥5 mm).

RESULT: Out of 52 samples received and with a total of 264 margins examined, the intraoperative frozen section demonstrated a sensitivity of approximately 79% and a specificity of about 98%. The positive predictive value was 86%, and the negative predictive value was 98%.

CONCLUSION: In our evaluation, we concluded that frozen section is a valuable intraoperative tool with high specificity but moderate sensitivity. It aids in identifying positive margins, allowing timely revision during surgery.

INTRODUCTION

Oral cancer is a major public health issue worldwide, and oral cavity cancers are among the most prevalent tumors in the world. India contributes a significant number of cases annually, especially in South and Southeast Asia, primarily due to the widespread usage of areca nut and tobacco [1,2]. Wide surgical excision is the main treatment approach with curative intent for solid oral squamous cell carcinoma (OSCC). The complete excision of the tumor along with a sufficient margin of surrounding healthy tissue is the primary objective of this procedure, which is essential to the results for the patient [3]. One of the most important independent prognostic factors in oral cancer surgery is the condition of the surgical margin. Tumor-free or "negative" margins greatly lower the incidence of local recurrence and boost overall and disease-free survival rates [4]. A margin is traditionally regarded as "close" if it is between 1 and 5 mm, "negative" if it is 5 mm or more and "positive" if it is less than 1 mm away from the invasive tumor boundary [5]. Sometimes, a positive or small margin calls for adjuvant treatments like chemotherapy or radiation therapy, which have their own side effects, or even a second, difficult re-resection. Thus, the capacity to precisely determine the status of the margin in real-time during the main surgical operation is extremely beneficial in clinical practice.

Intraoperative frozen section (IFS) analysis has become a widely used method to meet this need. A tissue sample obtained from the surgical margin is quickly frozen, sectioned, and stained during this treatment while the patient is still under anesthesia. Usually within 20 to 30 minutes, the pathologist uses a microscope to make a quick diagnosis, telling the surgeon if the margin is free of tumor cells. If malignant cells are discovered, the surgeon may immediately remove additional tissue from the positive region, aiming to get a definitive clear margin in a single procedure [7].

The diagnostic accuracy and usefulness of IFS, however, are still being debated and assessed despite its widespread usage and theoretical advantages. The technique has several drawbacks, one of which is the possibility of sampling errors, in which the small tissue sample examined does not accurately reflect the entire tissue and frozen artifacts that can alter cellular architecture, resulting in interpretive difficulties of margin [8,9]. The accuracy rate has varied widely across trials, with sensitivity rates changing considerably while specificity has remained consistently high [10,11]. Institutional self-assessment is crucial because the precision might vary depending on the pathologist's experience, the particular tumor subsite and institutional guidelines.

Considering the significant effects of margin status on a patient's outlook and future course of therapy, tertiary care facilities, which frequently handle complicated cases and sophisticated instances must pay close attention to it in order to analyze the effectiveness of their intraoperative evaluation methods. For this reason, this study was conducted to assess the diagnostic validity of intraoperative frozen section for margin, which includes the sensitivity, specificity, positive predictive value, and negative predictive value assessing oral cancer surgery at our institution by comparing its findings to the definitive results obtained via permanent histopathological analysis.

MATERIAL AND METHODS

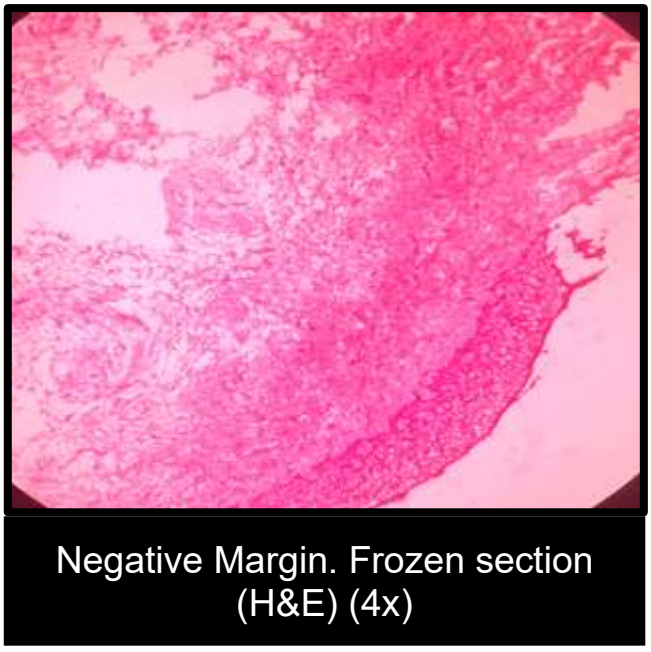
We conducted a retrospective study in the Department of Pathology at SRMS IMS, over a period of 1 year from June 2024 to May 2025. During the study period frozen sections of oral carcinoma were received for 54 patients. The tissues were taken as sample from all margins of the lesion, i.e. anterior, posterior, medial, lateral and deep, from patients who are undergoing surgical resection for malignancies. Also, each of the sample obtained were evaluated by both i.e. immediately prepared frozen sections and routine paraffin sections and then compared at last. All the surgical resection samples for oral carcinoma were considered except those with recurrence of oral cancer, prior treatment (such as biopsy, nodal biopsy, radiotherapy) and lack of positive histopathology diagnosis. All the frozen section margins immediately prepared were observed under light microscopy and margins were classified as “positive” if margin showed tumor deposits (invasive and in-situ), “close” when it is less then 5mm and “negative” when it is equal to or more than 5mm.

RESULTS AND OBSERVATION

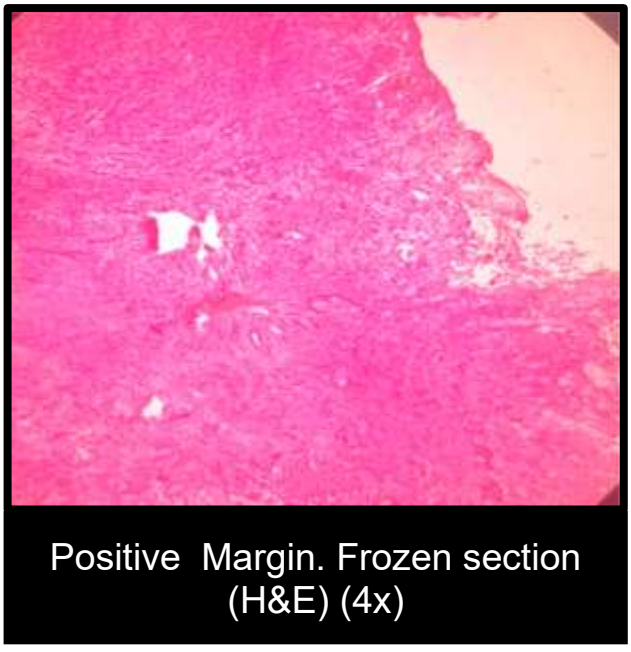
No. of cases	No. of margins evaluated	Presence of carcinoma in frozen section	Presence of carcinoma in paraffin section	Negative frozen section	Negative paraffin section
54	264	19	22	242	237

No. of cases	No. of margins examined	True positive	True negative	False positive	False negative
54	264	19	237	3	5

No. of margins	Sensitivity (%)	Specificity(%)	Positive predictive value(%)	Negative predictive value (%)	Efficiency (Accuracy)
264	79.17%	98.75%	86.36%	97.93%	96.97%



Negative Margin. Frozen section (H&E) (4x)



Positive Margin. Frozen section (H&E) (4x)

DISCUSSION

Complete oncologic resection with the surgical margin status being a key factor in determining patient outcomes, is the cornerstone of effective surgical treatment for oral squamous cell carcinoma [3,4]. A positive surgical margin is strongly indicative of local recurrence and is linked to lower survival rates, frequently requiring aggressive adjuvant therapy [6]. Intraoperative frozen section (IFS) analysis is an essential real-time instrument in this situation because it gives the surgeon an instantaneous microscopic evaluation of the margins. The main goal of this research was to compare IFS's diagnostic accuracy at our tertiary care facility to the gold standard of permanent histopathology. Our data indicate that IFS is a very helpful and precise instrument for the surgical treatment of oral cancer. In our cohort, the high specificity and negative predictive value(NPV) imply that IFS is extremely accurate when declaring a margin negative. On final pathology, it will probably be determined to be negative. This gives the surgeon a great deal of assurance to carry out reconstructive operations, reducing patient morbidity and avoiding needless surgery extensions. The high reliability

of a negative outcome is consistent with the results of numerous other investigations that have also demonstrated outstanding IFS specificity in head and neck cancer surgery [7,10]. In this scenario, having a high NPV is especially important since it lowers the chance of leaving residual tumor behind based on a false-negative result.

In contrast, the specificity of IFS in our trial was greater than its sensitivity, which, although helpful in clinical practice, was lower. This suggests the possibility of false-negative outcomes, where IFS was unable to identify the microscopic tumor presence that was later discovered on permanent sections. This is a well-known drawback of the approach [8,11]. Sampling error is frequently cited as the main factor behind false negatives. The pathologist is only able to analyze the tiny fragment of tissue that was sent for analysis and this may not be representative of the whole surgical margin. There may be a focus of malignancy in an adjacent, unsampled region of the margin. Additionally, if not included in the selected tissue specimen, microscopic "skip lesions" or discontinuous tumor spread might be overlooked. As the "Achilles' heel" of frozen section analysis, our findings concur with the larger body of research that recognizes sampling error [9].

We also had a few false-positive findings throughout our series. An incorrect positive diagnosis may result in the needless removal of more healthy tissue, which could make the patient's functional impairments worse. These mistakes are frequently interpretive and may be caused by artifacts that are introduced during the freezing procedure, which can alter tissue architecture and make it hard to distinguish invasive carcinoma from severe dysplasia or reactive alterations [8]. The low rate of false positives in our investigation indicates a high level of interpretative competence and supports the overall conclusion. Even though every false positive is clinically important, the positive predictive value (PPV) in our study was high, suggesting that a positive IFS finding is a reliable predictor of actual margin involvement which supports the surgeon's choice to re-excise and the reliability of the method as used by knowledgeable pathologists.

When comparing our findings to international standards, the accuracy rates at our institute are comparable to those reported from other major centers. For example, DiNardo et al. emphasized the usefulness of IFS in informing surgical choices and noted that they had achieved comparable overall accuracy [7]. The variance in reported sensitivity across Variations in institutional procedures for tissue sampling, tumor features and the particular subsites inside the oral cavity that are being investigated may be reflected in various investigations [10, 11]. This also highlights the importance of conducting its own quality assurance and regularly assessing the effectiveness of its IFS in each institution.

CONCLUSION

In conclusion, our research supports the use of intraoperative frozen section analysis as a highly accurate and dependable method for evaluating surgical borders during oral cancer surgery in a tertiary care environment. Its high negative predictive value offers essential reassurance to the surgeon, even if its sensitivity is constrained by underlying issues, notably sampling error. By allowing for the prompt surgical correction of positive margins, IFS continues to be an essential addition that maximizes the likelihood of a full resection in a single operation. To get the most out of the technique's clinical advantages, it's important that the surgeon and pathologist have a good understanding of its potential and constraints as well as effective communication.

LIMITATIONS

This study is not without its limitations. As a retrospective analysis from a single institution, the results may not be generalizable to all practice settings. Furthermore, the final determination of a "close" versus "positive" margin can sometimes be subject to inter-observer variability, even on permanent sections. Future research could prospectively evaluate standardized sampling protocols or incorporate novel intraoperative imaging techniques to complement IFS and potentially reduce sampling error.

Conflict of Interest: None.

Funding: None.
Ethical Approval: Not required.
Consent: Not required.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin*. 2021;71(3):209-249.
2. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F. Global Cancer Observatory: Cancer Today. Lyon, France: IARC; 2022.
3. Shah JP, Gil Z. The current concepts on the surgical management of oral cancer. *Oral Oncol*. 2009;45(4-5):394-401.
4. Sutton DN, Brown JS, Rogers SN, et al. The prognostic implications of the surgical margin in oral squamous cell carcinoma. *Int J Oral Maxillofac Surg*. 2003;32(1):30-34.
5. Woolgar JA, Triantafyllou A. A systematic review of the prognostic implications of the surgical margin in oral squamous cell carcinoma. *Oral Oncol*. 2017;72:50-59.
6. Bernier J, Cooper JS, Pajak TF, et al. Defining risk levels in locally advanced head and neck cancers: a comparative analysis of concurrent postoperative radiation plus chemotherapy trials of the EORTC (#22931) and RTOG (# 9501). *Head Neck*. 2005;27(10):843-850.
7. DiNardo LJ, Lin J, Karageorge LS, et al. Accuracy, utility, and cost of frozen section margins in head and neck cancer surgery. *Laryngoscope*. 2000;110(10 Pt 1):1773-1776.
8. Bulbul MG, Cicek E, Tatli U, et al. Does intraoperative frozen section analysis of surgical margins in oral cancer surgery really affect the local recurrence? A meta-analysis. *Oral Maxillofac Surg*. 2020;24(3):249-257.
9. Long SM, McLean T, Patel S, et al. Use of Intraoperative Frozen Section to Assess Final Tumor Margin Status in Patients Undergoing Surgery for Oral Cavity Squamous Cell Carcinoma. *JAMA Otolaryngol Head Neck Surg*. 2022;148(10):929–936.
10. Kumar A, Sharma S, Mohil RS, et al. Diagnostic accuracy of intraoperative frozen section for margin evaluation of oral cavity squamous cell carcinoma. *BMC Res Notes*. 2024;17(1):112.
11. Alvi A, Johnson JT. The role of frozen section in the management of squamous cell carcinoma of the head and neck. *Curr Opin Otolaryngol Head Neck Surg*. 1996;4(2):93-96.